

Retroviral Gene Therapy: May The Fibronectin Be With You

S. Louise Pay¹, Melanie Wurm², Cordula Leurs³, Dirk Lindemann⁴, Helmut Hanenberg¹

¹Wells Center for Pediatric Research, Indiana University School of Medicine, Indianapolis, IN

²Transfusion Medicine, Hannover Medical School, Hannover, Germany

³Pediatrics, Heinrich Heine University, Dusseldorf, Germany

⁴Virology, Technical University of Dresden, Dresden, Germany

Replication incompetent retroviral vectors are currently used in phase I clinical trials for genetic therapy of disorders of the blood and the immune system, as vector integration into the genome of target stem cells provides stable long-term expression of the therapeutic transgene. We have previously shown that co-localization of the viral particles and the target cells on the recombinant fibronectin fragment CH-296 enhances the retroviral gene transfer efficiency into primitive hematopoietic cells including stem cells. Here, we report additional technical details for improving the gene transfer efficiencies into hematopoietic cell lines, primary human T-cells and CD34+ cells and demonstrate that CH-296 can be used at least three times without any loss of efficiency. Finally, we expand the range of viral proteins known to directly bind to fibronectin CH-296 to the commonly used VSV-G, GaLV and foamyviral (FV) envelope.

Mentor: Helmut Hanenberg, Wells Center for Pediatric Research, Indiana University School of Medicine, Indianapolis, IN